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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/633,697 | 08/07/2000 | Gerard Andrew Potter | A33403PCT USA-A | 3756 |

21003 7590 12/05/2001

BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER

MCKENZIE, THOMAS C

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1624

DATE MAILED: 12/05/2001

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/633,697

Applicant(s)

POTTER ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 October 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 37-56 is/are pending in the application.
- 4a) Of the above claim(s) 53-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37-42, 44, 45, 47 and 49-52 is/are rejected.
- 7) ☒ Claim(s) 43, 46 and 48 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4, 8, 11, 13 6) ☐ Other: _____

DETAILED ACTION

1. This action is in response to an election of species and restriction filed on 10/11/01. There are twenty claims pending and sixteen under consideration. Claims 37-49 are compound claims. Claim 50 is a composition claim. Claim 51 is a method of preparation claim. Claim 52 is a use claim. The application concerns some benzyl and cinnamyl carbamate prodrugs. This is the first action on the merits.

Election/Restrictions

2. Claims 53-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16. The traversal was because the added search would not be burdensome. This is not persuasive because the different groups of inventions are in different US patent classes. Therefore, the search is burdensome. The requirement is still deemed proper and is therefore made FINAL.

3. Claims 37-41 and 49-52 are rejected on the grounds as being drawn to an improper Markush group *In re Harnisch* 206 USPQ 300. The claimed compounds, compositions, and methods that employ them present a variable core. Deletion of non-elected subject matter obviates this rejection. The Examiner suggests deleting reference to steroidal carbon framework and $n > \text{three}$.

Specification

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. The Examiner suggests the amended claim 37.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-42, 44, and 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The structural element in formula (Z) "Drug" is indefinite. Names, structures, and chemical formulas precisely define organic molecules. Attempting to define structure by function is not proper when the structures can be clearly expressed in terms that are more precise. It is not sufficient to define a chemical structure solely by its principal biological property. The Examiner suggests using the drug elements from the structures in claims 45 and 46, since that is what was searched.

6. Claims 37-42, 44, and 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "thiol" in the third to last line on page 2 is indefinite for two reasons. Firstly, a

thiol is a carbon-containing compound, not a univalent radical. Secondly, the term "thiol" is indefinite for it is not clear if the bond from the thiol group is from the sulfur. If the inventors intend the group HSR-, Examiner suggests the word "mercaptoalkyl". If they intend the group RS-, then the word "alkylthio" is appropriate. If the inventors intend the group HS-, Examiner suggests the word "mercapto". Any choice must be supported by the specification.

7. Claims 38-41, 44, and 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitations in claims 38-41 "wherein hydroxylation ... the drug moiety" is unduly functional. The limitation in claim 49 is also unduly functional. Names, structures, and chemical formulas precisely define organic molecules. Attempting to define structure by function is not proper when the structures can be clearly expressed in terms that are more precise. It is not sufficient to define a chemical structure solely by a biological property.

8. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 42 recites the limitation "a phenanthyl group" in the last line of the claim. There is no antecedent basis for

this limitation in claim 37. A phenanthrene is a fused, non-linear, tricyclic aromatic hydrocarbon. There is no way to form a tricyclic system from formula (Z) by joining R_2 and R_4 . Even if $n = 4$, there is no provision for fusing the second R_4 to anything, nor for that matter, anything left to fuse it to.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-41, 44, 47, and 49-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitations in claims 38-41 "wherein hydroxylation ... the drug moiety" is unduly functional. The limitation in claim 49 is also unduly functional. Which compounds possess these prosperities? How fast and to what extent must the enzymatic reactions occur so that a compound meets these claim limitations? How is this to be determined and how much experimentation must be employed to determine if a particular compound (or genus of thousands of compounds) are so metabolized?

10. Claim 52 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention. Applicants lack enablement for the treatment of cancer generally.

Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689.

The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "tumor" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

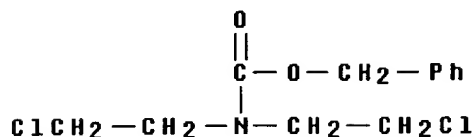
Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

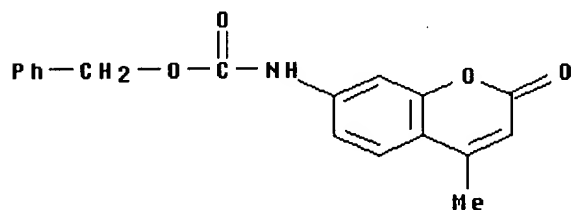
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

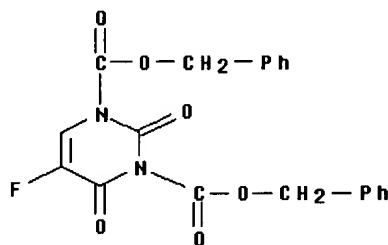
Claims 37-42 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Amble (Acta Chem. Scand.). The compound shown below fits formula (Z) with $X = R_1 = R_2 = R_3 = R_4 = \text{hydrogen}$, $n = 0$, A is absent, and drug = bis(2-chloroethyl)amine.. This also fits formula XX of claim 45. The compound is found in the diagram on page 585 and is compound 2a. Synthetic details are found in the paragraph spanning pages 585 to 586.



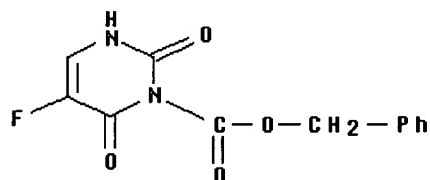
12. Claims 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Pamer (Mol. Biochem. Parasitol.). The compound shown below fits formula (Z) with $X = R_1 = R_2 = R_3 = R_4 = \text{hydrogen}$, $n = 0$, $A = \text{NH}$, and drug = 4-methyl-2-oxo-2H-1-benzopyran. The compound is found in and is called z-AMC and is disclosed in the footnote on the left side of page 27.



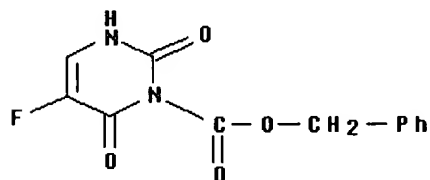
13. Claims 37-42, and 50-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Buur (Arch. Pharm. Chemi, Sci. Ed.). The compound shown below fits formula (Z) with $X = R_1 = R_2 = R_3 = R_4 = \text{hydrogen}$, $n = 0$, A is absent, and drug = N1-(benzyloxycarbonyl)-5-fluorouracil. An abstract of this publication is provided as the original is not readily available.



14. Claims 37-42, and 50-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Grelan Pharmaceutical Co. (JP 56/016474 A2). The compound shown below fits formula (Z) with $X = R_1 = R_2 = R_3 = R_4 = \text{hydrogen}$, $n = 0$, A is absent, and drug = 5-fluorouracil. The compound is named in the fifth line from the bottom of the right side of page 624.



15. Claims 37-42, and 50-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Suda (Biol. Pharm. Bull.). The compound shown below fits formula (Z) with $X = R_1 = R_2 = R_3 = R_4 = \text{hydrogen}$, $n = 0$, A is absent, and drug = 5-fluorouracil. An abstract of this publication is provided as the original is not readily available.

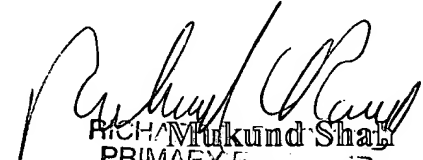


Allowable Subject Matter

16. Claims 43, 46, and 48 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

17. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for the Examiner is (703) 746-3152. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mukund Shah can be reached on (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.


MUKUND SHAH
PRIMARY EXAMINER
Supervisory Patent Examiner
Art Unit 1624

TCMcK
December 2, 2001

